



At Seedorf

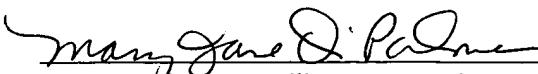
PATENT
ATTORNEY DOCKET NO. 50004/003004

Certificate of Mailing: Date of Deposit: April 13, 2000

I hereby certify under 37 CFR 1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated above and is addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231.

Mary Jane DiPalma

Printed name of person mailing correspondence


Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Roy A. Gravel et al.

Art Unit:

Serial No.: 09/487,841

Examiner:

Filed: January 19, 2000

Title: HUMAN METHIONINE SYNTHASE REDUCTASE: CLONING, AND METHODS FOR EVALUATING RISK OF NEURAL TUBE DEFECTS, CARDIOVASCULAR DISEASE, CANCER, AND DOWN'S SYNDROME

Assistant Commissioner of Patents

Washington, D.C. 20231

REPLY TO NOTICE TO FILE MISSING PARTS

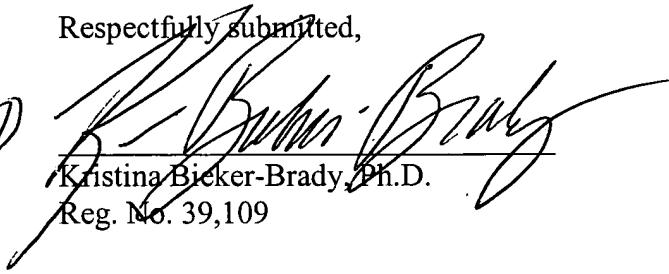
In reply to the Notice to File Missing Parts of Application mailed March 20, 2000 (a copy of which is enclosed), Applicant as a small entity submits herewith the following:

- A Combined Declaration and Power of Attorney in compliance with 37 CFR 1.63.
- Payment of the surcharge of \$65.00 for late filing of the basic filing fee/declaration.
- A signed small entity statement.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: April 12, 2000


Kristina Bicker-Brady, Ph.D.
Reg. No. 39,109

Clark & Elbing LLP

176 Federal Street

Boston, MA 02110

Telephone: 617-428-0200

Faxsimile: 617-428-7045

FORMALITIES LETTER



OC00000004998808

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark OfficeAddress: COMMISSIONER OF PATENT AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING/RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NUMBER
--------------------	---------------------	-----------------------	------------------------

09/487,841

01/19/2000

Rima Rozen

50004/003004

Kristina Bieker-Brady PhD
 Clark & Elbing LLP
 176 Federal Street
 Boston, MA 02110



Date Mailed: 03/20/2000

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given TWO MONTHS from the date of this Notice within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The oath or declaration is unsigned.
- To avoid abandonment, a late filing fee or oath or declaration surcharge as set forth in 37 CFR 1.16(e) of \$65 for a small entity in compliance with 37 CFR 1.27, must be submitted with the missing items identified in this letter.
- **The balance due by applicant is \$ 65.**

*A copy of this notice **MUST** be returned with the reply.*

Customer Service Center

Initial Patent Examination Division (703) 308-1202

PART 2 - COPY TO BE RETURNED WITH RESPONSE

04/19/2000 ASAHL 00000113 09487841

01 FC:205

65.00 OP



PATENT
ATTORNEY DOCKET NO. 50004/003004

Certificate of Mailing: Date of Deposit: April 13, 2000

I hereby certify under 37 CFR 1.8(a) that this correspondence is being deposited with the United States Postal Service as **first class mail** with sufficient postage on the date indicated above and is addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231.

Mary Jane DiPalma

Printed name of person mailing correspondence



Mary Jane DiPalma

Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Roy A. Gravel et al.

Art Unit:

Serial No.: 09/487,841

Examiner:

Filed: January 19, 2000

Title: HUMAN METHIONINE SYNTHASE REDUCTASE: CLONING, AND METHODS FOR EVALUATING RISK OF NEURAL TUBE DEFECTS, CARDIOVASCULAR DISEASE, CANCER, AND DOWN'S SYNDROME

Assistant Commissioner of Patents

Washington, D.C. 20231

PETITION TO CORRECT FILING RECEIPT

Applicant requests that the attached filing receipt be corrected as follows:

In the Applicant(s) section:

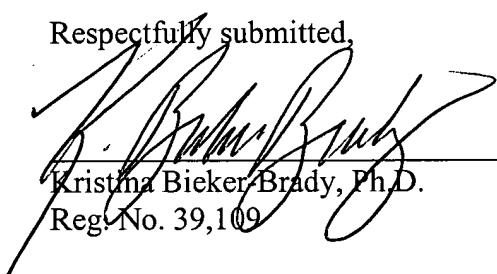
Above "Rima Rozen, Montreal, CANADA", insert --Roy A. Gravel, Alberta, CANADA--.

Attached are copies of the incorrect filing receipt and the Combined Declaration and Power of Attorney to note the first named inventor.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: April 17, 2000



Kristina Bieker-Brady, Ph.D.
Reg. No. 39,109

Clark & Elbing LLP

176 Federal Street

Boston, MA 02110

Telephone: 617-428-0200

Faxsimile: 617-428-7045

FILING RECEIPT

OC00000004998807


**UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office**

 Address: ASSISTANT SECRETARY AND
COMMISSIONER OF PATENT AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	DRAWINGS	TOT CLAIMS	IND CLAIMS
09/487,841	01/19/2000	1633	550	50004/003004	10	21	4

Kristina Bieker-Brady PhD
 Clark & Elbing LLP
 176 Federal Street
 Boston, MA 02110

MAR 23 2000 *CO* *bud*

Date Mailed: 03/20/2000

Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the PTO processes the reply to the Notice, the PTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

Applicant(s) *Roy A. Gravel, Alberta, CANADA*
 Rima Rozen, Montreal, CANADA;
 Daniel Leclerc, Montreal, CANADA;
 Aaron Wilson, Montreal, CANADA;
 David Rosenblatt, Montreal, CANADA;

Continuing Data as Claimed by Applicant

THIS APPLICATION IS A CIP OF 09/371,347 08/10/1999
 WHICH IS A CIP OF 09/232,028 01/15/1999
 AND CLAIMS BENEFIT OF 60/071,622 01/16/1998

Foreign Applications**If Required, Foreign Filing License Granted 03/20/2000****** SMALL ENTITY ******Title**

Human methionine synthetase reductase: cloning, and methods for evaluating risk of neural tube defects, cardiovascular disease, cancer, and down's syndrome

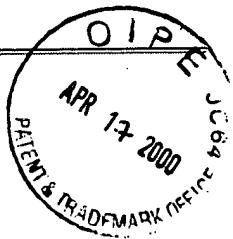
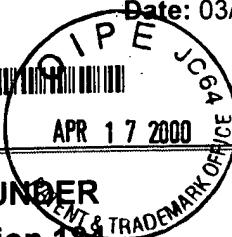
Preliminary Class

435

Data entry by : DILLON, LAWANDA

Team : OIPE

Date: 03/20/2000



**LICENSE FOR FOREIGN FILING UNDER
Title 35, United States Code, Section 184
Title 37, Code of Federal Regulations, 5.11 & 5.15**

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 36 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Office of Export Administration, Department of Commerce (15 CFR 370.10 (j)); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

PLEASE NOTE the following information about the Filing Receipt:

- The articles such as "a," "an" and "the" are not included as the first words in the title of an application. They are considered to be unnecessary to the understanding of the title.
- The words "new," "improved," "improvements in" or "relating to" are not included as first words in the title of an application because a patent application, by nature, is a new idea or improvement.
- The title may be truncated if it consists of more than 600 characters (letters and spaces combined).
- The docket number allows a maximum of 25 characters.
- If your application was submitted under 37 CFR 1.10, your filing date should be the "date in" found on the Express Mail label. If there is a discrepancy, you should submit a request for a corrected Filing Receipt along with a copy of the Express Mail label showing the "date in."

Any corrections that may need to be done to your Filing Receipt should be directed to:

Assistant Commissioner for Patents
Office of Initial Patent Examination
Customer Service Center
Washington, DC 20231